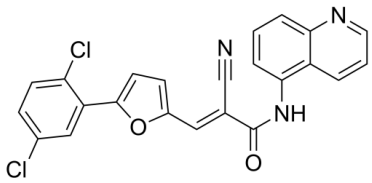
Data Sheet

Product Name:	AGK2
Cat. No.:	CS-7830
CAS No.:	304896-28-4
Molecular Formula:	$C_{23}H_{13}Cl_2N_3O_2$
Molecular Weight:	434.27
Target:	Apoptosis; Sirtuin
Pathway:	Apoptosis; Cell Cycle/DNA Damage; Epigenetics
Solubility:	DMSO : 12.5 mg/mL (ultrasonic)



BIOLOGICAL ACTIVITY:

AGK2 is a selective **SIRT2** inhibitor with an **IC_{50}** of 3.5 μM. AGK2 inhibits **SIRT1** and **SIRT3** with **IC_{50}**s of 30 and 91 μM, respectively. IC50 & Target: IC50: 3.5 μM (SIRT2), 30 μM (SIRT1), 91 μM (SIRT3)[1] ***In Vitro:*** AGK2 significantly inhibits cell proliferation in a dose-dependent manner. AGK2 also significantly inhibits cell growth in a dose-dependent manner without inducing cytotoxicity at low doses. Twelve days after AGK2 (5 μM) treatment, cells show a significantly reducing colony forming ability in soft agar to 46% of the control cells. Western blot analysis shows that the levels of CDK4 or CDK6 and cyclin D1 are decreased after AGK2 treatment in a dose-dependent manner. In addition, AGK2 inhibits the expression of p53 protein[2]. Treatment of microglial BV2 cells with 10 μM AGK2 leads to a significant increase in PAR signals. Treatment of microglial BV2 cells with 10 μM AGK2 also leads to a significant decrease in the intracellular ATP and significant increases in both late-stage apoptosis and necrosis of the cells[3]. ***In Vivo:*** AGK2 significantly reduces mortality and decreases levels of cytokines in blood (TNF-α: 298.3±24.6 vs 26.8±2.8 pg/mL, p=0.0034; IL-6: 633.4±82.8 vs 232.6±133.0 pg/mL, p=0.0344) and peritoneal fluid (IL-6: 704.8±67.7 vs 391.4±98.5 pg/mL, p=0.033) compare to vehicle control. AGK2 also suppresses the TNF-α and IL-6 production in the culturing splenocytes (TNF-α: 68.1±6.4 vs 23.9±2.8 pg/mL, p=0.0009; IL-6: 73.1±4.2 vs 49.6±3.0 pg/mL; p=0.0051)[4].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: AGK2 is dissolved in DMSO, which has a solubility of 10 mg/mL in DMSO[3].[2]Cells are exposed to different concentrations of AGK2 in 1 mL of 0.3% basal medium agar containing 10% FBS. The cultures are maintained at 37°C in a 5% CO_2 incubator for 10-15 days, and the cell colonies are scored using an inverted microscope[2]. **Animal Administration:** [4]Mice are intraperitoneally given either AGK2 (82 mg/kg) in dimethyl sulfoxide (DMSO) or DMSO alone, and 2 h later subjects to CLP. Survival is monitored for 240 hours. AGK2-treating mice are grouped into (i) DMSO vehicle, and (ii) AGK2, with sham mice (operating but without any treatment) serving as controls. Peritoneal fluid and peripheral blood are examined at 24 and 48 hours for cytokine production[4].

References:

[1]. Tatum PR, et al. Identification of novel SIRT2-selective inhibitors using a click chemistry approach. Bioorg Med Chem Lett. 2014 Apr 15;24(8):1871-4.

[2]. Kim HW, et al. Sirtuin inhibitors, EX527 and AGK2, suppress cell migration by inhibiting HSF1 protein stability. Oncol Rep. 2016 Jan;35(1):235-42.

[3]. Li Y, et al. Poly(ADP-ribose) polymerase mediates both cell death and ATP decreases in SIRT2 inhibitor AGK2-treated microglial BV2 cells. Neurosci

Lett. 2013 Jun 7;544:36-40.

[4]. Zhao T, et al. Selective Inhibition of SIRT2 Improves Outcomes in a Lethal Septic Model. Curr Mol Med. 2015;15(7):634-41.

CAIndexNames:

2-Propenamide, 2-cyano-3-[5-(2,5-dichlorophenyl)-2-furanyl]-N-5-quinolinyl-

SMILES:

O=C(NC1=C2C=CC=NC2=CC=C1)/C(C#N)=C/C3=CC=C(C4=CC(Cl)=CC=C4Cl)O3

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